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Low Birth Weight and Increased Sympathetic Activity

To the Editor:

In a recent study on twins, IJzerman et al¹ report an association between low birth weight and a short pre-ejection period at rest and during stress tests. They interpret their findings as evidence for an increased sympathetic nervous activity in low birth weight subjects. These data elucidate an important aspect in the regulation of the sympathetic system in low birth weight subjects. However, on the background of a study of our group, which examined muscle sympathetic nerve activity (MSNA) in low birth weight singletons,² the interpretation of the results may have to be modified. In our study, sympathetic neural activity to the muscle vascular bed was determined by specific intraneural measurement. Under resting conditions, MSNA was lower in low birth weight subjects as compared with a control group with normal birth weight. Baroreflex function was also examined and showed normal functional properties. Additionally, sympathoexcitatory maneuvers (inspiratory apnea and cold pressor test) enhanced sympathetic activity in low birth weight subjects to the same extent as in control subjects.

The different results could be explained by the difference in cohorts studied. Whereas IJzerman examined monozygotic and dizygotic twins, we compared sympathetic regulation in low birth weight singletons in a case-control design. The fetal growth pattern of twins differs from that of singletons. The growth deceleration in twins occurs particularly in the last trimester of pregnancy, indicating that fetoplacental insufficiency is a major pathogenetic factor.³ In contrast, low birth weight singletons are rather affected during the whole fetal period, and maternal factors seem to play a predominant role. As indicated by results of animal studies, the effect of intrauterine growth restriction on the sympathetic nervous system depends on both the mode and the timing of the adverse event in utero.⁴

Both the IJzerman et al¹ study and our study show that intrauterine insults affect the regulation of sympathetic functions. However, the finding of an increased sympathetic activity to the heart does not automatically imply an activation of other branches of the sympathetic nervous system. In fact, one can hypothesize that baroreflex regulation is responsible for the findings of both studies. Thus, the enhanced cardiac sympathetic activity could be counterbalanced by lower sympathetic outflow to the muscle vascular bed or vice versa. The significance for developing arteriosclerotic risk factors, however, remains to be determined.

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differences in birth weight in singletons. Of course, intrauterine growth in twins is different from that in singletons in several respects. However, the association between birth weight and blood pressure in the overall sample of twins (-1.9 mm Hg per kg increase of birth weight) was remarkably similar to the well-established association in singletons (approximately -2 mm Hg per kg increase of birth weight).¹ The same holds true for the size of the association of birth weight with serum lipids² in the overall sample of twins, which was similar to the size of the association in singletons.³ In addition, differences in birth weight within twin pairs have been associated with differences in many variables that have been related to birth weight in singletons, such as blood pressure, diabetes, serum lipids, fibrinogen, myocardial infarction and height (for references see IJzerman et al⁴). Although intrauterine growth in twins may be different from that in singletons, the associations between birth weight and cardiovascular risk in twins suggest that birth weight in twins is relevant for the development of cardiovascular disease and that differences in birth weight in twins can be used as a model for differences in birth weight in singletons.

We agree with Weitz et al⁵ that an increased sympathetic activity to the heart does not automatically imply an activation of other branches of the sympathetic nervous system. They argue that, in subjects with a low birth weight, baroreflex regulation is responsible for enhanced cardiac sympathetic activity as well as lower sympathetic outflow to the muscle vascular bed. This is an intriguing and testable working hypothesis. However, sympathetic activity to the heart, as measured in our study ($n=228$), is probably more relevant with respect to the development of high blood pressure than sympathetic activity to the leg. Finally, in the study by Weitz et al⁵ ($n=20$), birth weight was not associated with blood pressure. This makes it questionable whether the individuals studied by Weitz et al were an "appropriate" sample to investigate potential mechanisms (such as sympathetic activity) linking birth weight to blood pressure.

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Response

We thank Weitz et al for their comments. They argue that differences in birth weight in twins are a poor model for

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